

CLAIMS

1. A method for diagnosing a person's susceptibility for having an increased risk for the development of atherosclerosis, said method comprising determining whether
5 said subject has a polymorphism in the signal peptide part of the human preproNPY, said polymorphism comprising the substitution of the position 7 leucine for proline in the signal peptide part of said preproNPY, said polymorphism being indicative of an increased risk for the development of atherosclerosis.

10 2. The method according to claim 1 wherein said person has diabetes.

3. A method for diagnosing a diabetic person's susceptibility for having an increased risk for the development of diabetic retinopathy, said method comprising
15 determining whether said subject has a polymorphism in the signal peptide part of the human preproNPY, said polymorphism comprising the substitution of the position 7 leucine for proline in the signal peptide part of said preproNPY, said polymorphism being indicative of an increased risk for the development of diabetic retinopathy.

20 4. A method for treating a person, diagnosed for having an increased risk for the development of atherosclerosis according to claim 1 or 2, for the prevention of developing atherosclerosis, comprising administering to said person an effective amount of an agent counteracting the influence of the mutated NPY gene.

25 5. The method according to claim 4 wherein said agent is a pharmaceutical aimed to modulate synthesis, secretion or metabolism of the endogenous NPY, or to interact in a specific manner at NPY target sites by modulating effects of NPY with specific NPY receptor proteins.

6. The method according to claim 4 wherein said agent is a pharmaceutical aimed to modulate gene expression of normal or mutated NPY gene.

7. A method for treating a person, diagnosed for having an increased risk for the development of atherosclerosis according to claim 1 or 2, for the prevention of developing atherosclerosis, comprising subjecting the person to specific gene therapy aimed to repair the mutated NPY sequence.

8. A method for treating a diabetic person, diagnosed for having an increased risk for the development of diabetic retinopathy according to claim 3, for the prevention of developing diabetic retinopathy, comprising administering to said person an effective amount of an agent counteracting the influence of the mutated NPY gene.

9. The method according to claim 8 wherein said agent is a pharmaceutical aimed to modulate synthesis, release or metabolism of the endogenous NPY, or to interact in a specific manner at NPY target sites by modulating effects of NPY with specific NPY receptor proteins.

10. The method according to claim 8 wherein said agent is a pharmaceutical aimed to modulate gene expression of normal or mutated NPY gene.

11. A method for treating a diabetic person, diagnosed for having an increased risk for the development of diabetic retinopathy according to claim 3, for the prevention of developing diabetic retinopathy, comprising subjecting the person to specific gene therapy aimed to repair the mutated NPY sequence.

12. A method to investigate or screen pharmaceuticals or genetic aims useful in the treatment of atherosclerosis or diabetic retinopathy, by using an animal model including a transgenic animal which carries a human DNA sequence comprising a

nucleotide sequence encoding a prepro-neuropeptide Y (preproNPY) or part thereof encoding mature human NPY peptide, where the leucine amino acid in position 7 of the signal peptide part of said preproNPY i) is unchanged or ii) has been replaced by proline.

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13. A method to investigate or screen pharmaceuticals or genetic aims useful in the treatment of atherosclerosis or diabetic retinopathy, by using an animal model including a transgenic animal, which carries a DNA sequence comprising a nucleotide sequence encoding otherwise normal mouse NPY sequence or part thereof encoding mature mouse NPY peptide, but in which the nucleotide sequence encoding the mouse signal peptide is replaced by human signal peptide sequence encoding either normal or mutated human signal peptide.

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